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Original Article

Physiology Section

Prevalence of Sarcopenia in Liver Cirrhosis Patients and Determinants of Survival in Cirrhotic Population: A Prospective Cohort Study

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ABSTRACT

Introduction: Chronic liver diseases are the leading cause of mortality and are associated with a significant reduction in health-related quality of life, as well as being a major complication in cirrhosis. There is a high risk of reduced muscle mass, muscle strength, or function, known as sarcopenia, in patients with liver cirrhosis. Sarcopenia is a major determinant of survival in cirrhosis patients, along with the Child-Turcotte Pugh (CTP) score and the Model for End-stage Liver Disease (MELD) scores.

Aim: To study the prevalence of sarcopenia in patients with liver cirrhosis by assessing skeletal muscle mass using the third lumbar level Skeletal Muscle Index (SMI) through Computed Tomography (CT) and to determine the survival analysis of the cohort using a Cox regression model.

Materials and Methods: The present study was a prospective cohort study conducted in the Department of Gastroenterology and Hepatology at Sree Gokulam Medical College and Research Foundation in Thiruvananthapuram, Kerala, India, from October 2018 to October 2022. A total of 209 patients with cirrhosis were evaluated. Liver biochemical parameters, CTP score, and the MELD score were studied. Age, gender, and aetiology were noted. All subjects were assessed for sarcopenia using CT at the third lumbar vertebrae level SMI, and all subjects were followed-up every six months for survival. Survival curves and survival probability were evaluated for all the subjects recruited in the present study. Cumulative survival rates were estimated by the Kaplan-Meier method for sarcopenia, CTP score, and the MELD scores after categorisation into the aetiology of cirrhosis, and the groups were compared using the Log-rank test. Independent factors associated with mortality were identified using Cox proportional hazards models. A p-value <0.05 was considered statistically significant.

Results: The mean age±Standard Deviation of the subjects was 58.24±9.9 years. Among the subjects, males accounted for 161 (77%), while 48 (23%) were females. In subjects with sarcopenia (n=77), the survival rate was 53 (68.8%), and in subjects without sarcopenia (n=132), the survival rate was significantly higher at 110 (83.3%) with a p-value <0.05 (p=0.027). Univariate Cox regression analysis indicated that sarcopenia was a statistically significant predictor of survival. The mortality risk was higher in individuals with sarcopenia, with a Hazard Ratio (HR) of 1.9 and a 95% Confidence Interval (CI) ranging from 1.1-1.4. In the Cox regression model, CTP class B/C had a 2.4 times higher risk for mortality than CTP class A (p<0.05). Individuals with sarcopenia had a 1.76 times higher risk of mortality compared to those without (HR=1.765, 95% CI: 0.983-3.17) in the multivariate Cox regression analysis. Aetiology and CTP class scores were independently associated with mortality (p<0.05) after adjusting for multiple prognostic factors in the multivariate Cox regression analysis.

Conclusion: Univariate Cox regression analysis indicated that sarcopenia was a statistically significant predictor of survival, with a higher mortality risk in individuals with sarcopenia. The multivariate Cox regression model for survival concluded that CTP class B/C posed a higher risk for mortality compared to CTP class A.

Keywords: Aetiology, Child-Turcotte-Pugh, Model for end stage liver disease

INTRODUCTION

Chronic diseases of the liver are the major morbidity worldwide and in the Asia Pacific region. It is the leading cause of mortality and is associated with a significant reduction in health-related quality of life [1]. Sarcopenia is a major complication of cirrhosis and has high morbidity and mortality. The prevalence of sarcopenia varies from 23-60% and is more commonly observed among individuals with Alcoholic Liver Disease (ALD) and males [2,3]. Sarcopenia is characterised by the progressive loss of skeletal muscle mass, a decrease in skeletal muscle strength, and reduced physical endurance [4,5].

Clinical practice guidelines of the European Association for the Study of the Liver (EASL) [6] and the European Society for Clinical Nutrition and Metabolism (ESPEN) [7] recommend screening for sarcopenia among individuals with cirrhosis. Early recognition is a critical aspect of caring for patients with liver cirrhosis [8]. Sarcopenia in cirrhosis is a predictor of complications such as infections, hepatic encephalopathy, and reduced survival, making it an important prognostic factor for survival [9,10].

There were only a very few studies from Indian literature on the prevalence and consequences of sarcopenia among individuals with cirrhosis of the liver [11-13]. In the present study, the prevalence of sarcopenia among patients with liver cirrhosis of all aetiologies was evaluated using quantitative assessment of normative values and cut-offs of SMI, and they were prospectively followed-up for survival. Factors such as CTP score and MELD scores were evaluated [14].

MATERIALS AND METHODS

The present study was a prospective cohort study conducted in the Department of Gastroenterology and Hepatology of Sree Gokulam Medical College and Research Foundation, Thiruvanathapuram, Kerala, India from October 2018 to October 2022. The present

study was approved by the Institutional Ethics Committee (SGMC-IEC No: 31/382/11/2018) and was performed in accordance with the Helsinki Declaration of 1975. Informed consent was obtained from each participant to participate in the study.

Sample size calculation: The sample size was calculated based on the following assumptions. According to Hara N et al., using the Asian cutoffs, the prevalence of sarcopenia in cirrhosis was 25% [15], and Tandon P et al., used European cutoffs, with a prevalence of 41% [16]. Hence, the estimated prevalence of sarcopenia was found to be 32.5%, between 25% and 41%. The calculated sample size was 199 subjects, and with a possible loss to follow-up of 5%, hence, 209 subjects with liver cirrhosis were enrolled.

Inclusion criteria: Subjects diagnosed with cirrhosis between the ages of 18 to 70 years based on physical examination, imaging studies {abdominal ultrasound/Computed Tomography (CT) scan of the abdomen}, laboratory tests, liver stiffness by transient elastography, and upper gastrointestinal endoscopy for portal hypertension were included in the study [13].

Exclusion criteria: Subjects with liver cancer, other malignancies, and patients with human immunodeficiency virus, tuberculosis, chronic obstructive pulmonary disease, chronic renal failure, congestive heart failure, neuromuscular disorders, and inflammatory bowel disease were excluded.

Study Procedure

All subjects were evaluated for liver biochemical parameters. The CTP score and the MELD score were used to assess the functional status as a composite measure for liver function assessment. The CTP is a scoring system used to assess the prognosis of chronic liver disease, including cirrhosis, composed of factors such as total bilirubin level, serum albumin, International Normalised Ratio (INR), degree of ascites, and degree of hepatic encephalopathy. There were three distinct groups based on the scoring system ranging from 5-15. Scores between 5 and 8 were grouped into CTP class A (less severe), scores 9-11 were in CTP class B (moderately severe), and scores between 12-15 were in CTP class C (most severe) [17].

The MELD score is used as a severity scoring system in chronic liver disease and an excellent three-month mortality predictor, consisting of serum bilirubin, serum creatinine, and the INR for prothrombin time to predict three-month survival, with scores ranging from 6 to 40. A higher MELD score is associated with increasing severity of hepatic dysfunction and an increased 3-month mortality risk [18].

Data were collected on demographic features such as age, gender, aetiology, CTP, and MELD scores. All subjects were evaluated for skeletal muscle mass and later followed-up every six months. The mean duration of follow-up was four years from October 2018 to October 2022 until mortality or being recorded as lost to follow-up. Based on complications in cirrhosis, subjects were divided into Compensated Cirrhosis (CC) (no complications) and Decompensated Cirrhosis (DC) group (with complications).

Skeletal Muscle Index (SMI) using Computed Tomography (CT): Assessment of skeletal muscle mass was done using the cross-sectional images of CT, known as the gold standard tool for assessing sarcopenia [19]. At the lumbar (L3) level, the visualised total skeletal muscles included the psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal obliques, and rectus abdominis muscles. The lumbar (L3) level was considered an excellent indicator of whole-body muscle mass. Hence, skeletal muscle mass was assessed and measured using CT imaging at the L3 level in sarcopenia research [20]. Using computer software and with Hounsfield unit thresholds of 29 to 150, skeletal muscles were identified and measured. Since skeletal muscle volume strongly correlated with height, it was normalised for the height (cm^2/m^2) of the subjects. Thus, the SMI calculated was used in the current study to diagnose sarcopenia [21].

There are heterogeneities in the cut-offs for diagnosing sarcopenia by CT, by measuring the cross-sectional area of abdominal SMI normalised to the height of the patient at the third Lumbar vertebra (L3) [22]. Cirrhotic patients are considered sarcopenic when L3-SMI is <50 cm^2/m^2 in males and <39 cm^2/m^2 in females based on the Western cut-off [23], or <36.5 cm^2/m^2 for males and <30.2 cm^2/m^2 for females according to the Asian cut-off [11]. According to quantitative assessment of normative values of skeletal muscle indices in the Indian population, the cut-off values for L3-SMI are <39.59 cm^2/m^2 in males and <31.83 cm^2/m^2 in females [14], and the same cut-offs were used in the present study. CT images for cross-sectional skeletal muscle mass assessment were analysed at the level of lumbar 3 by a single observer using the National Institutes of Health Image J (Java) 1.5.3 software [24]. For muscle tissue, standard attenuation values ranged from 29 to 150 Hounsfield units. The cross-sectional areas achieved were normalised for patient height, obtaining the SMI, which is expressed as a cross-sectional muscle area/$height^2$ and was carried out by an experienced radiologist following guidelines [22].

STATISTICAL ANALYSIS

The IBM Stastical Packages for Social Sciences (SPSS) statistics for windows, Version 24.0, Armonk, New York (NY), was used for statistical analysis. Categorical data such as sex and aetiology of cirrhosis were presented as frequencies and percentages, while continuous data such as age, duration of survival, CTP score, and the MELD scores were summarised with means and standard deviations. Cumulative survival rates were estimated by the Kaplan-Meier method for sarcopenia, age, CTP score, and the MELD scores after categorisation into aetiology of cirrhosis, and the groups were compared using the Log-rank test. Independent factors associated with mortality were identified using Cox proportional hazards models. A p-value <0.05 was considered statistically significant, and all statistical tests were two-tailed.

RESULTS

There were 209 subjects; 185 (88.5%) had Compensated Cirrohosis (CC) and 24 (11.5%) had complications classified as Decompensated Cirrhosis (DC). The mean (±SD) age of participants was 58.24±9.9 years. Among the aetiologies, 128 (61.2%) had ALD [Table/Fig-1]. In CC, 112 (60.5%) had ALD and 52 (28.1%) had NASH; in DC, 16 (66.7%) had ALD and 5 (25%) had NASH. In CC, 100 (54.1%) were child A, while the rest were child B and C - 85 (45.9%), compared to DC where 14 (58.3%) were child B and C and 10 (41.7%) were in child A. The MELD score of 9+ was higher in DC than in CC (p=0.05) [Table/Fig-2].

Variables		Number (%)
Cirrhosis	Compensated	185 (88.5)
	Decompensated	24 (11.5)
Gender	Male	161 (77)
	Female	48 (23)
Aetiology	Alcohol Liver Disease (ALD)	128 (61.2)
	Hepatitis B Virus (HBV)	17 (8.1)
	Hepatitis C Virus (HCV)	5 (2.4)
	Non Alcoholic Steatohepatitis (NASH)	58 (27.8)
	Auto-immune Hepatitis (AIH)	1 (0.5)

[Table/Fig-1]: Baseline characteristics of subjects with cirrhosis.

Using the Indian cut-offs of L3-SMI, sarcopenia was observed in 77 subjects (36.8%). From [Table/Fig-3], it was evident that there was a higher proportion of sarcopenia (n=50) among those with ALD (total n=128) compared to NASH (n=17) (p=0.043). Similarly, Child B and C functional status subjects (total n=99) had higher sarcopenia (n=44) compared to those with Child A (n=33) (p=0.031). Those with

Variables		Compensated cirrhosis (n=185)		Decompensated cirrhosis n=24		Total (N=209)		*p-value
		n	%	n	%	n	%	
Aetiology	ALD	112	60.5	16	66.7	128	61.2	0.827
	NASH	52	28.1	6	25	58	27.8	
	HBV, HCV, AIH	21	11.4	2	8.3	23	11	
Severity scores	Child A	100	54.1	10	41.7	110	52.6	0.253
	Child B/C	85	45.9	14	58.3	99	47.4	
	MELD <9	99	53.8	8	33.3	107	51.4	0.05
	MELD >9	86	46.5	16	66.7	102	48.8	

[Table/Fig-2]: Aetiology and severity scores in compensated and decompensated cirrhosis.
*Chi-square test with df=1

Variables		Sarcopenia present (n=77)		Sarcopenia absent (n=132)		Total (N=209)		*p-value
		n	%	n	%	n	%	
Aetiology	ALD	50	64.9	78	59.1	128	61.2	*0.043
	NASH	17	22.1	41	31.1	58	27.8	
	HBV, HCV, AIH	10	13	13	9.8	23	11	
Severity scores	Child A	33	42.9	77	58.3	110	52.6	**0.031
	Child B/C	44	57.1	55	41.7	99	47.4	
	MELD <19	63	82.9	122	92.4	185	88.5	***0.033
	MELD >19	14	18.2	10	7.6	24	11.5	

[Table/Fig-3]: Aetiology and severity scores in cirrhotics with sarcopenia and without sarcopenia sarcopenia.
Chi-square test- *6.3, df=2, **χ^2 4.7 df=1, ***χ^2=4.5 with df=1

a MELD score greater than 19 (total n=24) had more sarcopenia (n=14) compared to those with MELD <19 (p=0.033).

The Log-rank test indicated a statistically significant difference in survival between individuals with and without sarcopenia, with p=0.029 showing significance. Individuals with sarcopenia appeared to have a shorter mean survival duration compared to those without sarcopenia, supported by the Chi-squared statistic [Table/Fig-4]. The univariate Cox regression analysis revealed sarcopenia as a statistically significant predictor of survival. The mortality risk was higher in individuals with sarcopenia, with an Hazard Ratio (HR) of 1.9 and a 95% confidence interval ranging from 1.1 to 1.4 [Table/Fig-5].

Sarcopenia	Number (%)	Death	Survived n (%)	Duration of survival (years)* Mean	SE	95% CI
No	132 (63.15)	22	110 (83.30)	12.9	0.713	11.5-14.3
Yes	77 (36.8)	24	53 (68.80)	11.8	1.265	9.35-14.3
Total	209 (100)	46	163 (78.00)	13.7	0.78	12.1-15.2

[Table/Fig-4]: Sarcopenia and survival duration.
*Log-rank test: Chi-squared 4.92, df=1; p=0.029

Mortatily risk	B	SE	Wald	df	p-value	HR	95% CI for HR
Sarcopenia	0.644	0.295	4.752	1	0.029	1.9	1.1-1.4

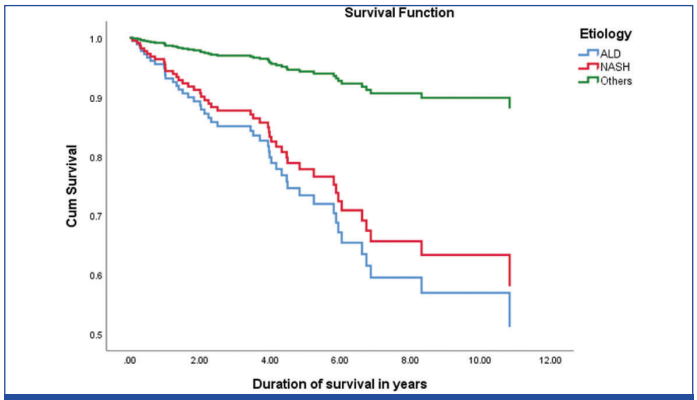
[Table/Fig-5]: Mortality risk of sarcopenia.

There was no statistically significant difference in survival between individuals aged <60 years and >60 years (p>0.05). The difference in survival between males and females was also not statistically significant (p>0.05) [Table/Fig-6].

[Table/Fig-7] indicated that among all aetiologies of cirrhosis, ALD had the lowest survival rate, followed by NASH-related cirrhosis, with p=0.035.

Variables		Total	Death n	Alive n (%)	Duration of survival* Estimate	SE	95% Confidence interval	p-value
Age (years)	<60	125	26	99 (79.2)	13.960	0.976	12.048-15.872	0.259
	>60	84	20	64 (76.2)	9.474	0.728	8.049-10.900	
	Overall	209	46	163 (78.0)	13.668	0.780	12.138-15.197	
Gender	Male	161	37	124	11.496	0.700	10.124-12.869	0.726
	Female	48	9	39	15.315	1.303	12.762-17.868	
	Overall	209	46	163	13.668	0.780	12.138-15.197	

[Table/Fig-6]: Survival analysis by age, gender and survival duration in years.
*Log-rank test: Chi-squared 1.276, df=1. **Log-rank test: Chi-squared 0.122, df=1



[Table/Fig-7]: Kaplan-Meier survival analysis by aetiology (Y axis-Cumulative survival).

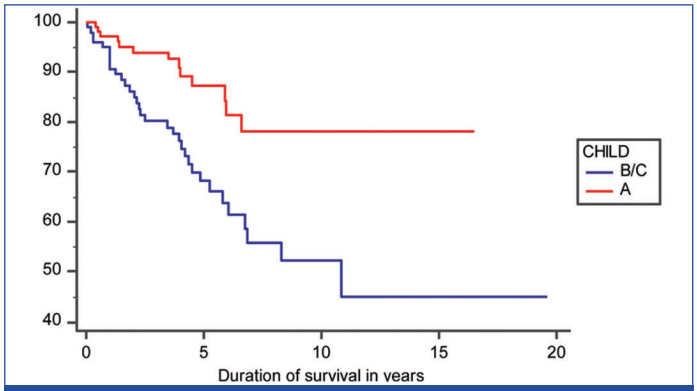
Cox regression analysis revealed that individuals with ALD had a significantly higher HR of mortality compared to the other aetiology groups [Table/Fig-8].

Aetiology	B	SE	Wald	Df	p	HR	95% CI for HR Lower bound	Upper bound
Others (HBV/HCV/AIH) (Ref category)			5.255	2	0.072			
Alcohol Liver Disease (ALD)	1.661	0.732	5.144	1	0.023	5.27	1.25	22.12
NASH	1.452	0.773	3.53	1	0.06	4.27	0.94	19.42

[Table/Fig-8]: Cox regression for aetiology.

[Table/Fig-9,10] demonstrated that cirrhotics with Child class B/C had the lowest survival rate compared to those with Child class A.

The Log-rank test showed a statistically significant difference in survival between CTP class A and class B/C, with a 2.75 times higher hazard of mortality in the CTP class B/C category compared to the CTP class A category (p<0.05) [Table/Fig-11,12].



[Table/Fig-9]: Survival analysis by Child Turcotte Pugh (CTP).

CHILD	Total	Mortality	Survived*	
			n	Percentage
A	110	13	97	88.2%
B or C	99	33	66	66.7%
Overall	209	46	163	78.0%

[Table/Fig-10]: Survival analysis by Child-Turcotte Pugh (CTP).
p=0.001 p-value <0.001

CHILD	Duration of survival			
	Mean	SE	95% Confidence interval*	
			Lower bound	Upper bound
A	13.791	0.716	12.388	15.194
B and C	11.413	1.139	9.180	13.645
Overall	13.668	0.780	12.138	15.197

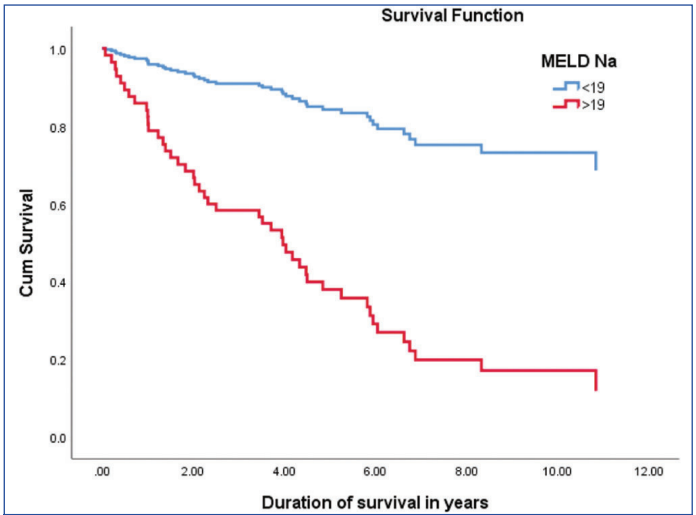
[Table/Fig-11]: Survival duration by Child-Turcotte Pugh (CTP) class.
*Log-rank (Mantel-Cox) Chi-squared 10.34 with 1 df and p<0.001

CTP class	B	SE	Wald	Df	p	HR	95% CI for HR	
							Lower bound	Upper bound
B and C (ref A)	1.01	0.328	9.509	1	0.002	2.75	1.45	5.215

[Table/Fig-12]: Cox Regression showing Hazard Ratio (HR) for child pugh class (CTP class).

[Table/Fig-13] indicated that in subjects with Model for End-stage Liver Disease Sodium (MELD Na) >19, the survival rate was lower compared to subjects with MELD Na <19.

[Table/Fig-14] displayed that the survival rate of subjects with MELD Na above 19 was the lowest compared to subjects with MELD Na <19.



[Table/Fig-13]: Survival by MELD Na.

MELD Na	Total N	Events number	Censored	
			N	Percent
<19	186	30	156	83.9%
>19	23	16	7	30.4%
Overall	209	46	163	77.99%

[Table/Fig-14]: Survival and MELD Na19.
p<0.001

Survival duration by MELD Na showed a Log-rank (Mantel-Cox) Chi-squared value of 38.732 (1 df) and a p<0.001. The HR for mortality was 5.65 times higher in the MELD Na >19 category compared to the MELD Na <19 category [Table/Fig-15,16].

The Cox regression model, Chi-square statistics indicated that the overall model had a -2 Log likelihood of 414.6 with 4 degrees of freedom (df) and a p-value of 0.001. CTP class B/C had 2.4 times more risk for mortality than CTP class A (p=0.01). Sarcopenia

MELD Na	Duration of survival			
	Estimate	Std. error	95% Confidence interval*	
			Lower bound	Upper bound
<19	15.290	0.771	13.779	16.801
>19	4.411	0.708	3.024	5.798
Overall	13.750	0.782	12.218	15.283

[Table/Fig-15]: Survival duration and MELD Na 19.
*Log-rank (Mantel Cox) Chi-squared 38.732 with 1 df and p <0.001

MELD Na	B	SE	Wald	df	p-value	HR	95% CI for HR	
							Lower bound	Upper bound
>19	1.732	0.314	30.383	1	0	5.65	3.05	10.46

[Table/Fig-16]: Cox regression showing Hazard Ratio (HR) MELD Na >19.

subjects had a 1.77 times higher risk of mortality than non sarcopenic individuals in the multivariate Cox regression analysis. Aetiology and CTP class scores were independently associated with mortality (p<0.05) after adjusting for multiple prognostic factors in the multivariate Cox regression analysis [Table/Fig-17].

Variables	B	SE	Wald	df	p	Hazard Ratio (HR)	95.0% CI for HR	
							Lower bound	Upper bound
CTP class B and C versus A	0.862	0.333	6.688	1	0.01	2.368	1.232	4.551
Sarcopenia	0.568	0.299	3.616	1	0.057	1.765	0.983	3.17
Aetiology (HBV/HCV/ AIH)-Ref category			4.53	2	0.104			
Alcohol Liver Disease (ALD)	0.099	0.35	0.08	1	0.778	0.906	0.456	1.8
Non-alcoholic steatohepatitis (NASH)	1.565	0.735	4.53	1	0.033	0.209	0.049	0.884

[Table/Fig-17]: Multivariate Cox regression model for survival.

DISCUSSION

In the present study, sarcopenia was observed in 77 (36.8%) out of 209 cirrhosis patients, and the risk of mortality was higher in those with sarcopenia compared to those without it. In a recent study by Khan S et al., in 2022, among 111 subjects with critically ill cirrhosis, 76 (68.5%) had sarcopenia, and the mortality rate was higher (72.4%) in those with sarcopenia compared to those without (40%). There was a 1.7 times higher risk for sepsis and a four-fold risk of mortality in the ICU [25]. Hormonal imbalance, altered nutrient metabolism, decreased protein intake, and hyperammonemia contribute to sarcopenia, leading to a higher risk of cirrhosis complications and increased mortality [26]. According to a meta-analysis of 4,037 patients, sarcopenia was linked to an increased risk of infection and longer hospital stays. Sarcopenia was associated with lower survival in cirrhosis patients, independent of other risk factors such as age and MELD score [27]. Differences in racial characteristics, body size, dietary habits, and quality of life vary between Asian and Western populations in different countries, leading to higher mortality rates. Even after height adjustment, the mean muscle mass of Asians is approximately 15% lower than that of Westerners [28].

In a recent meta-analysis by Zhang X-M et al., involving fourteen studies with 3,249 participants, the prevalence of sarcopenia ranged from 22 to 72 percent, with a pooled prevalence of 41% and a 95% CI of 33-49%. This prevalence aligns with the findings of the present study. Individuals with sarcopenia had a 2.28 times higher risk of mortality compared to those without sarcopenia, across various

types of mortality such as in-hospital mortality, 30-day mortality, and 1-year mortality [29]. In the present study, individuals with sarcopenia had a HR of 1.9 with a 95% confidence interval ranging from 1.1 to 1.4.

In a retrospective study of 104 patients with liver cirrhosis, sarcopenia (38.5%) in combination with CTP class B/C (26.9%) was associated with a worsened prognosis. The survival rate was significantly lower in patients with both sarcopenia and CTP B/C class within this group [30]. A systematic review on survival in cirrhosis revealed lower survival rates in cirrhotics with CTP class B/C compared to those with Child class A [31]. In another retrospective study focusing on osteosarcopenia and prognosis of cirrhosis without hepatocellular carcinoma, osteosarcopenia was identified as an independent risk factor in patients with liver cirrhosis. Child class B/C and MELD score were associated with higher mortality in univariate analysis. Child B/C with HR 7.045 and osteosarcopenia with HR 4.798 were recognised as independent prognostic factors ($p<0.001$). The cumulative survival rate at one, three, and five years was lowest among individuals with osteosarcopenia in Child B/C and osteosarcopenia [32]. A retrospective study of 1174 cirrhotic patients showed decreased survival in those with alcohol-related cirrhosis [33], consistent with the findings of the present study. Among 452 liver cirrhosis patients in Korea, 190 had sarcopenia with a prevalence of 42%. Mortality was higher in patients with sarcopenia and a MELD score ≥15, with a HR of 2.253 ($p<0.005$) [34]. Similarly, the present study demonstrated higher mortality in individuals with sarcopenia as well as a MELD >19.

The present study estimated the prevalence of sarcopenia by assessing muscle mass with CT L3 SMI using Indian cut-offs. The present prospective cohort study of cirrhotics with and without sarcopenia, followed-up for four years for mortality and analysed for survival using Cox regression analysis, identified these as strengths of the study. Administering nutrition and physical activity in cirrhotics with and without sarcopenia and examining their survival in a large cohort would be a future research recommendation.

Limitation(s)

The present study calculated the sample size based on the best estimate, and with the current sample size, the HR has been evaluated. A larger sample size could have provided a higher HR for the present study. The present study did not take co-morbidities into consideration, which could have an effect on the rate of survival in subjects.

CONCLUSION(S)

The mortality risk was higher in those with sarcopenia than without in univariate regression analysis. Using the univariate model, sarcopenia resulted in an increased risk of mortality and indicated that sarcopenia was a statistically significant predictor of survival. The mortality risk was higher in individuals with sarcopenia and had a high HR. In cirrhotics, CTP class B/C had a higher hazard for mortality compared to those in CTP class A. Similarly, MELD Na over 19 had a higher mortality hazard than MELD Na <19. Multivariate Cox regression analysis concluded that aetiology and CTP class were independently associated with mortality.

REFERENCES

[1] Prasad S, Dhiman RK, Duseja A, Chawla YK, Sharma A, Agarwal R. Lactulose improves cognitive functions and health-related quality of life in patients with cirrhosis who have minimal hepatic encephalopathy. Hepatology. 2007;45(3):549-59. Doi: 10.1002/hep.21533.

[2] Bunchorntavakul C, Reddy KR. Review article: Malnutrition/sarcopenia and frailty in patients with cirrhosis. Aliment Pharmacol Ther. 2019;51(1):64-77. Doi: 10.1111/apt.15571.

[3] Hari A. Muscular abnormalities in liver cirrhosis. World J Gastroenterol. 2021;27(29):4862-78. Doi: 10.3748/wjg.v27.i29.4862.

[4] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European consensus on definition and diagnosis. Age and Ageing. 2018;48(1):16-31. Doi: 10.1093/ageing/afy169.

[5] Cruz-Jentoft AJ, Sayer AA. Sarcopenia. The Lancet. 2019; 393(10191):2636-46. Doi: 10.1016/s0140-6736(19)31138-9.

[6] Merli M, Berzigotti A, Zelber-Sagi S, Dasarathy S, Montagnese S, Genton L, et al. EASL clinical practice guidelines on nutrition in Chronic liver disease. J Hepatol. 2019;70(1):172-93. Doi: 10.1016/j.jhep.2018.06.024.

[7] Bischoff SC, Bernal W, Dasarathy S, Merli M, Plank LD, Schütz T, et al. Espen practical guideline: Clinical nutrition in liver disease. Clin Nutr. 2020;39(12):3533-62. Doi: 10.1016/j.clnu.2020.09.001.

[8] Periyalwar P, Dasarathy S. Malnutrition in cirrhosis: Contribution and consequences of sarcopenia on metabolic and clinical responses. Clin Liver Dis. 2012;16(1):95-131. Doi: 10.1016/j.cld.2011.12.009.

[9] Lai JC, Tandon P, Bernal W, Tapper EB, Ekong U, Dasarathy S, et al. Malnutrition, frailty, and sarcopenia in patients with cirrhosis: 2021 practice guidance by the American Association for the study of liver diseases. Hepatology. 2021;74(3):1611-44. Doi: 10.1002/hep.32049.

[10] Shiraki M, Nishiguchi S, Saito M, Fukuzawa Y, Mizuta T, Kaibori M, et al. Nutritional status and quality of life in current patients with liver cirrhosis as assessed in 2007-2011. Hepatol Res. 2013;43(2):106-12. Doi: 10.1111/hepr.12004.

[11] Anand A, Mohta S, Agarwal S, Sharma S, Gopi S, Gunjan D, et al. European Working Group on sarcopenia in older people (EWGSOP2) criteria with population-based skeletal muscle index best predicts mortality in Asians with cirrhosis. J Clin Exp Hepatol. 2022;12(1):52-60. Doi: 10.1016/j.jceh.2021.03.015.

[12] Thyloor Kenchappa S, Sharma S, Kumar M, Ghuman SS, Arora A, Ranjan P. A prospective study of prevalence and impact of sarcopenia on short-term mortality in hospitalised patients with liver cirrhosis. J Clin Exp Hepatol. 2023;13(6):946-54. Doi:10.1016/j.jceh.2023.05.001.

[13] Evuri P, Selvi C, Manimekala E, Aravind A, Karunakaran P, Muthukumaran K, et al. Study of prevalence of sarcopenia in chronic liver disease and its impact on outcomes. Int J Innov Res Med Sci. 2022;7(7):335-39. Doi: 10.23958/ijirms/vol07-i07/1439.

[14] Choudhary S, Wadhawan M, Dhawan S, Ganesan PK, Mittal P, Sahney A, et al. Normative values of skeletal muscle indices for nutritional assessment and implications on definition of sarcopenia in Indian adult population. Indian J Gastroenterol. 2022;41(1):69-76. Doi: 10.1007/s12664-021-01207-2.

[15] Hara N, Iwasa M, Sugimoto R, Mifuji-Moroka R, Yoshikawa K, Terasaka E, et al. Sarcopenia and sarcopenic obesity are prognostic factors for overall survival in patients with cirrhosis. Intern Med. 2016;55(8):863-70. Doi: 10.2169/internalmedicine.55.5676. Epub 2016 Apr 15. PMID: 27086797.

[16] Tandon P, Ney M, Irwin I, Ma MM, Gramlich L, Bain VG, et al. Severe muscle depletion in patients on the liver transplant wait list: Its prevalence and independent prognostic value. Liver Transpl. 2012;18(10):1209-16. Doi: 10.1002/lt.23495. PMID: 22740290.

[17] Durand F, Valla D. Assessment of the prognosis of cirrhosis: Child-pugh versus meld. J Hepatol. 2005;42 Suppl(1):S100-07. Doi: 10.1016/j.jhep.2004.11.015.

[18] Emenena I, Emenena B, Kweki A, Aiwuyo HO, Osarenkhoe JO, Iloeje UN, et al. Model for End Stage Liver Disease (MELD) score: A tool for prognosis and prediction of mortality in patients with decompensated liver cirrhosis. Cureus. 2023;15(5):e39267. Doi: 10.7759/cureus.39267.

[19] Tagliafico AS, Bignotti B, Torri L, Rossi F. Sarcopenia: How to measure, when and why. Radiol Med. 2022;127(3):228-37. Doi: 10.1007/s11547-022-01450-3.

[20] Son SW, Song DS, Chang UI, Yang JM. Definition of sarcopenia in chronic liver disease. Life. 2021;11(4):349. Doi: 10.3390/life11040349.

[21] Bai J, Xu M, Peng F, Gong J, Zhao J, Song X, et al. Skeletal muscle mass index as a predictor of long-term cirrhosis onset in young non cirrhotic males with acute-on-chronic liver failure. Front Nutr. 2022;9:1071373. Doi: 10.3389/fnut.2022.1071373.

[22] Ebadi M, Bhanji RA, Dunichand-Hoedl AR, Mazurak VC, Baracos VE, Montano-Loza AJ. Sarcopenia severity based on computed tomography image analysis in patients with cirrhosis. Nutrients. 2020;12(11):3463. Doi: 10.3390/nu12113463.

[23] Carey EJ, Lai JC, Wang CW, Dasarathy S, Lobach I, Montano-Loza AJ, et al. A multicentre study to define sarcopenia in patients with end-stage liver disease. Liver Transplantation. 2017;23(5):625-33. Doi:10.1002/lt.24750.

[24] Lee CM, Kang BK, Kim M. Radiologic definition of sarcopenia in chronic liver disease. Life (Basel). 2021;11(2):86. Doi: 10.3390/life11020086. PMID: 33504046; PMCID: PMC7910987.

[25] Khan S, Benjamin J, Maiwall R, Tripathi H, Kapoor PB, Shasthry V, et al. Sarcopenia is the independent predictor of mortality in critically ill patients with cirrhosis. J Clin Trans Res. 2022;8(3):200-08. Doi: 10.18053/jctres.08.202203.006.

[26] Traub J, Reiss L, Aliwa B, Stadlbauer V. Malnutrition in patients with liver cirrhosis. Nutrients. 2021;13(2):540. Doi: 10.3390/nu13020540.

[27] Kim G, Kang SH, Kim MY, Baik SK. Prognostic value of sarcopenia in patients with liver cirrhosis: A systematic review and meta-analysis. PLOS ONE. 2017;12(10):0186990. Doi: 10.1371/journal.pone.0186990.

[28] Puri P, Dhiman RK, Taneja S, Tandon P, Merli M, Anand AC, et al. Nutrition in chronic liver disease: Consensus statement of the Indian National Association for Study of the Liver. J Clin Exp Hepatol. 2021;11(1):97-143. Doi: 10.1016/j.jceh.2020.09.003.

[29] Zhang XM, Chen D, Xie XH, Zhang JE, Zeng Y, Cheng AS. Sarcopenia as a predictor of mortality among the critically ill in an intensive care unit: A systematic review and meta-analysis. BMC Geriatrics. 2021;21(1):339. Doi: 10.1186/s12877-021-02276-w.

[30] Saeki C, Kanai T, Ueda K, Nakano M, Oikawa T, Torisu Y, et al. Prognostic significance of sarcopenia and severe vitamin D deficiency in patients with cirrhosis. JGH Open. 2023;7(5):351-57. Doi: 10.1002/jgh3.12900.

[31] D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. J Hepatol. 2006;44(1):217-31. Doi: 10.1016/j.jhep.2005.10.013.

[32] Saeki C, Kanai T, Ueda K, Nakano M, Oikawa T, Torisu Y, et al. Osteosarcopenia predicts poor survival in patients with cirrhosis: A retrospective study. BMC Gastroenterology. 2023;23(1):196. Doi: 10.1186/s12876-023-02835-y.
[33] Choi C, Choi DH, Spears GM, Peeraphatdit T (Bee), Serafim LP, Gajic O, et al. Relationship between aetiology of cirrhosis and survival among patients hospitalised in Intensive Care Units. Mayo Clinic Proceedings. 2022;97(2):274-84. Doi: 10.1016/j.mayocp.2021.08.025.
[34] Kang SH, Jeong WK, Baik SK, Cha SH, Kim MY. Impact of sarcopenia on prognostic value of cirrhosis: Going beyond the hepatic venous pressure gradient and meld score. J Cachexia Sarcopenia Muscle. 2018;9(5):860070. Doi: 10.1002/jcsm.12333.

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